

IN THE CLAIMS

- 1-3 (canceled)
4. (currently amended) A composition for generating an immune response in a mammal, said composition comprising:
- (a) a polycistronic polynucleotide component comprising:
- a first polynucleotide sequence comprising a first coding sequence for a first HIV immunogenic polypeptide; and
- a second polynucleotide sequence comprising a second coding sequence for a second HIV immunogenic polypeptide, wherein the first and second HIV immunogenic polypeptides are derived from different HIV strains, and
- (b) a polypeptide component comprising a third HIV immunogenic polypeptide which is analogous to the first and second polypeptides, with the proviso that if the polypeptide component comprises two or more HIV immunogenic polypeptides, then at least one of the two or more HIV immunogenic polypeptides is derived from a different HIV strain than the first and second HIV immunogenic polypeptides.
5. (withdrawn—previously presented) The composition according to claim 4, wherein the first and second HIV immunogenic polypeptides are derived from different HIV strains of the same subtype.
6. (withdrawn—previously presented) The composition according to claim 5, wherein the first, second, and third HIV immunogenic polypeptides are derived from HIV strains of the same subtype.

7. (previously presented) The composition according to claim 4, wherein the first and second coding sequences are derived from HIV strains of different subtypes.
8. (previously presented) The composition according to claim 4, wherein the third HIV immunogenic polypeptide is derived from an HIV strain of a different subtype than the first and second HIV immunogenic polypeptides.
- 9-11 (canceled)
12. (currently amended) The composition of claim ~~[[1]]~~ 4, wherein said polynucleotide component is a native polynucleotide or the second HIV immunogenic polypeptide is a native polypeptide.
13. (currently amended) The composition of claim ~~[[1]]~~ 4, wherein said polynucleotide component is a synthetic polynucleotide.
14. (original) The composition of claim 13, wherein said synthetic polynucleotide comprises codons optimized for expression in mammalian cells.
15. (original) The composition of claim 14, wherein said synthetic polynucleotide comprises codons optimized for expression in human cells.

16-29. (canceled)

30. (currently amended) The composition of claim [[1]] 4, wherein said polynucleotide component further comprises a ~~second~~ third polynucleotide sequence encoding one or more additional antigenic polypeptides which are not derived from an HIV-1 strain.
31. (previously presented) The composition of claim 30, wherein said polypeptide component further comprises an additional antigenic peptide which is not derived from an HIV-1 strain.
32. (currently amended) The composition of claim [[1]] 4, wherein said polynucleotide component further comprises a control element compatible with expression in a selected host cell and operably linked to the polynucleotide sequence encoding the first HIV immunogenic polypeptide.
33. (previously presented) The composition of claim 32, wherein said control element is selected from the group consisting of a transcription promoter, a transcription enhancer element, a transcription termination signal, a polyadenylation sequence, a sequence for optimization of initiation of translation, an internal ribosome entry site, and a translation termination sequence.
34. (previously presented) The composition of claim 33, wherein said transcription promoter is selected from the group consisting of a CMV promoter, a CMV+intron A promoter, an

SV40 promoter, an RSV promoter, an HIV-Ltr promoter, an MMLV-ltr promoter, and a metallothionein promoter.

35. (withdrawn—currently amended) A method of generating an immune response in a subject, comprising administering the composition of claim [[1]] 4 to said subject under conditions that are compatible with expression of the first and second HIV immunogenic polypeptides ~~polypeptide~~.

36-37. (canceled)

38. (withdrawn—previously presented) The method of claim 35, wherein said polypeptide component further comprises an adjuvant.

39. (withdrawn—previously presented) The method of claim 35, wherein said polynucleotide component further comprises a carrier.

40. (withdrawn—previously presented) The method of claim 35, wherein the polynucleotide component comprises a nonviral vector.

41. (withdrawn—previously presented) The method of claim 35, wherein the polynucleotide component is delivered using a particulate carrier.

42. (canceled)

43. (withdrawn— previously presented) The method of claim 35, wherein the polynucleotide component is delivered using a PLG particle.
44. (withdrawn—previously presented) The method of claim 35, wherein the polynucleotide component is encapsulated in a liposome preparation.
45. (withdrawn—previously presented) The method of claim 44, wherein the polynucleotide component comprises a viral vector.
46. (withdrawn—previously presented) The method of claim 45, wherein the viral vector is selected from the group consisting of a retrovirus vector, a lentivirus vector, an alphavirus vector, and an adenovirus vector.
- 47-49. (canceled)
50. (withdrawn— previously presented) The method of claim 46, wherein the viral vector is an adenovirus vector.
51. (withdrawn—previously presented) The method of claim 50 wherein the adenovirus vector is a live replicating vector.

52. (withdrawn—previously presented) The method of claim 50 wherein the adenovirus vector is a non-replicating vector.
53. (withdrawn) The method of claim 35, wherein said subject is a mammal.
54. (withdrawn) The method of claim 53, wherein said mammal is a human.
55. (withdrawn) The method of claim 35, wherein said immune response comprises an adaptive immune response.
56. (withdrawn) The method of claim 55 wherein said immune response further comprises an innate immune response.
57. (withdrawn—previously presented) The method of claim 35, wherein the immune response is selected from the group consisting of an Antibody Dependent Cell Mediated Cytotoxic response, a humoral immune response, a cellular immune response, and combinations thereof.
- 58-59. (canceled)
60. (withdrawn—previously presented) The method of claim 35, wherein the polynucleotide component is administered intramuscularly, intramucosally, intranasally, subcutaneously, intradermally, transdermally, intravaginally, intrarectally, orally or intravenously.

61. (withdrawn—previously presented) The method of claim 35, wherein said immune response results in generating neutralizing antibodies in the subject against multiple strains derived from the one or more of said HIV subtypes.
62. (canceled)
63. (withdrawn) The method of claim 35 wherein said immune response comprises the in vivo generation in said subject of broadly neutralizing antibodies that neutralize multiple HIV isolates.
64. (withdrawn) The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity to HIV strains utilizing the CCR5 coreceptor.
65. (withdrawn) The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from the same HIV subtype.
66. (withdrawn—currently amended) The method of claim 65 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV strains selected from the group consisting of a Bal HIV isolate, a JR-FL HIV isolate, a Bx08 HIV isolate,

a 6101 HIV isolate, a 692 HIV isolate, a 1168 HIV isolate, a 1196 HIV isolate, and an ADA HIV isolate.

67. (withdrawn) The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from two or more different HIV subtypes.
68. (withdrawn—previously presented) The method of claim 67 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV subtypes selected from the group consisting of HIV subtypes A, B, C, D, E, F, G, and O.
69. (withdrawn) The method of claim 35 wherein said immune response comprises the generation in said subject of antibodies that mediate Antibody Dependent Cell Mediated Cytotoxicity (ADCC).
70. (withdrawn) The method of claim 69 wherein said antibodies are characterized in that they demonstrate ADCC activity against two or more HIV strains from two or more different HIV subtypes.
71. (withdrawn—previously presented) The method of claim 70 wherein said antibodies demonstrate ADCC activity against two or more HIV subtypes selected from the group consisting of HIV subtypes A, B, C, D, E, F, G, and O.

72. (withdrawn) The method of claim 69 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from the same HIV subtype.
73. (withdrawn—currently amended) The method of claim 69 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV strains selected from the group consisting of a Bal HIV isolate, a JR-FL HIV isolate, a Bx08 HIV isolate, a 6101 HIV isolate, a 692 HIV isolate, a 1168 HIV isolate, a 1196 HIV isolate, and an ADA HIV isolate.
- 74-78. (canceled)
79. (currently amended) The composition according to claim ~~[[1]]~~ 4, wherein said polypeptide component is expressed on a virus like particle.
- 80-83. (canceled)
84. (previously presented) The composition of claim 4, wherein the first and second HIV immunogenic polypeptides comprise HIV envelope polypeptides.
85. (currently amended) The composition of claim 4, wherein at least one of the ~~polynucleotide component, the first HIV-immunogenic polypeptide, and/or the second~~

~~HIV immunogenic polypeptide or the third HIV immunogenic polypeptides~~ comprises an alteration or a mutation.

86. (previously presented) The composition of claim 85, wherein said alteration or mutation is selected from the group consisting of (1) a mutation in the cleavage site; (2) a mutation in the glycosylation site; (3) a deletion of the V1 region; (4) a modification of the V1 region; (5) a deletion in the V2 region; (6) a modification of the V2 region; (7) a deletion of the V3 region; (8) a modification of the V3 region; (9) a mutation that exposes a neutralizing epitope of the HIV Env polypeptide; and (10) combinations thereof.
87. (previously presented) The composition of claim 85, wherein at least one of the first and second said HIV immunogenic polypeptides comprises an Env polypeptide modified to expose a CD4 binding region or an envelope binding region that binds to a CCR5 chemokine co-receptor.
88. (previously presented) The composition of claim 4, wherein the first HIV immunogenic polypeptide is selected from the group consisting of: Gag, Env, Pol, Protease (Prot), Integrase (Int), Reverse Transcriptase (RT), Vif, Vpr, Vpu, Tat, Rev, and Nef.
89. (previously presented) The composition of claim 4, wherein the first HIV strain is an HIV subtype selected from the group consisting of: subtype A, subtype B, subtype C, subtype D, subtype E, subtype F, subtype G, subtype H, subtype I, subtype J, subtype K, subtype N and subtype O.

90. (canceled).